Remarks/Arguments

Claims 13, 15-18, 20, and 23 are amended. Claims 22 and 25 are canceled. Claims 1-2, 4-5, 7-13, 15-18, 20-21, and 24-25 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Claim Rejections Under 35 USC § 102

A. Claims 1, 5, 7-13, 17-18, and 20-25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lecomte, et al. (Int. J. Cancer, vol. 100, pp. 542-548, 2002). Claims 22 and 25 have been canceled without prejudice, thus the rejection against these claim are now moot.

Claims 1, 5, 7-13, 17-18, 20, and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated. Applicant respectfully traverses this rejection.

Independent claims 1, 7, 9, 11, 17-18, 20, and 23 are drawn to methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample. Likewise, independent claim 13 as amended is drawn to methods of detecting LOH and DNA hypermethylation in a bone marrow sample.

Applicant respectfully submits that Lecomte fails to disclose or teach a methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample, as required by claims 1, 7, 9, 11, 17-18, 20, and 23. In contrast, Lecomte discloses methods using peripheral blood (p. 543, col. 1, paragraph 2). Therefore, Lecomte does not teach or suggest the method of claims 1, 7, 9, 11, 17-18, 20, and 23.

Accordingly, Lecomte does not anticipate the present claims 1, 7, 9, 11, 17-18, 20, and 23. Likewise, dependent claims 5, 8, 10, 12, 21, and 24 are also patentable over Lecomte for at least the same reasons as claims 1, 7, 9, 11, 17-18, 20, and 23.

In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

In addition, Lecomte fails to disclose or teach a methods of detecting LOH and DNA hypermethylation in a bone marrow sample, as required by claim 13 16. In contrast, Lecomte discloses methods using peripheral blood (p. 543, col. 1, paragraph 2). Therefore, Lecomte does not teach or suggest the method of claim 13.

Accordingly, Lecomte does not anticipate the present claim 13. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

B. Claims 1-2, 5, 7, 9, 11, 13, 17-18, 20, 22-23, and 25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Bearzatto, et al. (Clin Can Res, vol. 8, pp. 3782-3787, Dec. 2002). Claims 22 and 25 have been canceled without prejudice, thus the rejection against these claim are now moot.

Claims 1-2, 5, 7, 9, 11, 13, 17-18, 20, and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated. Applicant respectfully traverses this rejection.

Independent claims 1, 7, 9, 11, 17-18, 20, and 23 are drawn to methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample. Likewise, independent claim 13 as amended is drawn to methods of detecting LOH and DNA hypermethylation in a bone marrow sample.

Applicant respectfully submits that Bearzatto fails to disclose or teach a methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample, as required by claims 1, 7, 9, 11, 17-18, 20, and 23. In contrast, Bearzatto discloses methods using peripheral blood (p. 3783, col. 1, paragraph 2). Therefore, Bearzatto does not teach or suggest the method of claims 1, 7, 9, 11, 17-18, 20, and 23.

Accordingly, Bearzatto does not anticipate the present claims 1, 7, 9, 11, 17-18, 20, and 23. Likewise, dependent claims 5 and 8 are also patentable over Bearzatto for at least the same reasons as claims 1, 7, 9, 11, 17-18, 20, and 23. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

In addition, Bearzatto fails to disclose or teach a methods of detecting LOH and DNA hypermethylation using a bone marrow sample, as required by claim 13. In contrast, Bearzatto discloses methods using peripheral blood (p. 3783, col. 1, paragraph 2). Therefore, Bearzatto does not teach or suggest the method of claim 13.

Accordingly, Bearzatto does not anticipate the present claims 13. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

C. Claims 1, 5, 7, 9, 11, 13, 17-18, 20, 22-23, and 25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Dominguez, et al. (Clin Caner Res, vol. 8, pp. 980-985, Apr. 2002). Claims 22 and 25 have been canceled without prejudice, thus the rejection against these claim are now moot.

Claims 1-2, 5, 7, 9, 11, 13, 17-18, 20, and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated. Applicant respectfully traverses this rejection.

Independent claims 1, 7, 9, 11, 17-18, 20, and 23 are drawn to methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample. Likewise, independent claim 13 as amended is drawn to methods of detecting LOH and DNA hypermethylation in a bone marrow sample.

Applicant respectfully submits that Dominguez fails to disclose or teach a methods of detecting, staging, prognosing cancer by detecting DNA markers in a

bone marrow sample, as required by claims 1, 7, 9, 11, 17-18, 20, and 23. In contrast, Dominguez discloses methods using peripheral blood (p. 980, col. 2, paragraph 3). Therefore, Dominguez does not teach or suggest the method of claims 1, 7, 9, 11, 17-18, 20, and 23.

Accordingly, Dominguez does not anticipate the present claims 1, 7, 9, 11, 17-18, 20, and 23. Likewise, dependent claim 5 is also patentable over Dominguez for at least the same reasons as claims 1, 7, 9, 11, 17-18, 20, and 23. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

In addition, Dominguez fails to disclose or teach a methods of detecting LOH and DNA hypermethylation using a bone marrow sample, as required by claim 13. In contrast, Dominguez discloses methods using peripheral blood (p. 980, col. 2, paragraph 3). Therefore, Dominguez does not teach or suggest the method of claim 13.

Accordingly, Dominguez does not anticipate the present claim 13. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

D. Claims 9-13, 15, 17-18, and 20-25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Silva, et al. (Annals of Surgical Oncology, vol. 9(1), pp. 71-76, 2002). Claims 22 and 25 have been canceled without prejudice, thus the rejection against these claim are now moot.

Claims 9-13, 15, 17-18, 20-21, and 23-24 stand rejected under 35 U.S.C. § 102(b) as being anticipated. Applicant respectfully traverses this rejection.

Independent claims 9, 11, 17-18, 20, and 23 are drawn to methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow

sample. Likewise, independent claims 13 and 15 as amended are drawn to methods of detecting LOH and DNA hypermethylation in a bone marrow sample.

Applicant respectfully submits that Silva fails to disclose or teach a methods of detecting, staging, prognosing cancer by detecting DNA markers in a bone marrow sample, as required by claims 9, 11, 17-18, 20, and 23. In contrast, Silva discloses methods using peripheral blood (p. 72, col. 1, paragraph 3). Therefore, Silva does not teach or suggest the method of claims 9, 11, 17-18, 20, and 23.

Accordingly, Silva does not anticipate the present claims 9, 11, 17-18, 20, and 23. Likewise, dependent claims 5, 8, 10, 12, 21, and 24 are also patentable over Silva for at least the same reasons as claims 9, 11, 17-18, 20, and 23. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

In addition, Silva fails to disclose or teach a methods of detecting LOH and DNA hypermethylation using a bone marrow sample, as required by claims 13 and 15. In contrast, Silva discloses methods using peripheral blood (p. 72, col. 1, paragraph 3). Therefore, Silva does not teach or suggest the method of claims 13, 15, and 16.

Accordingly, Silva does not anticipate the present claims 13 and 15. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Claim Rejections Under 35 USC § 103

A. Claim 4 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Lecomte in view of Silva. Applicant respectfully traverses this rejection

Claim 4 depends from independent claim 1, and as such includes all the limitations thereof, and is therefore patentable over Lecomte for at least the same reasons discussed above with regard to claim 1. Silva is not seen to remedy the

defects of Lecomte and is cited for its relevance regarding DNA markers (abstract, p. 72, col. 2, paragraph 3). As such, the combined teachings of the prior art fail to teach or suggest each element of the claimed invention. Thus, the combination suggested by the Office cannot render the claimed invention obvious.

The Examiner indicates that it would have been obvious to one skilled in the art to modify the method for detecting DNA markers in cancer samples as taught by Lecomte with the DNA markers taught by Silva because of the reasonable expectation of success that the combination of methods would result in a sensitive method for detecting cancer. Applicant respectfully submits that the combined methods still fail to teach or suggest methods of detecting DNA markers in bone marrow sample, as required by claim 1.

Accordingly, Lecomte in view of Silva is not obvious over the present claim 1. Likewise, dependent claim 4 is also patentable over Lecomte in view of Silva for at least the same reasons as claim 1. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

B. Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Silva in view of Kawakami, et al.(J. Natl. Cancer Institute, vol. 92, no. 22, 2000). Applicant respectfully traverses this rejection.

Claim 16, has been amended as follows:

> A method of detecting LOH and DNA hypermethylation, comprising
>
> providing a cell-free bone marrow sample from a subject; and
>
> detecting a combination of LOH and DNA hypermethylation in the sample, wherein the DNA

hypermethylation is detected in RASSF1A, MGMT, GSTP1, RAR-ß, TWIST, APC, DAPK, or Cyclin D2 promoter.

Applicant respectfully submits that Silva fails to disclose or teach methods of detecting LOH and DNA hypermethylation in a bone marrow sample. Kawakami is not seen to remedy the defects of Silva and is cited for its relevance regarding the hypermethylation of DNA markers. As such, the combined teachings of the prior art fail to teach or suggest each element of the claimed invention. Thus, the combination suggested by the Office cannot render the claimed invention obvious.

The Examiner indicates that it would have been obvious to one skilled in the art to modify the method for detecting DNA markers in cancer samples as taught by Silva with the DNA markers taught by Kawakami because of the reasonable expectation of success that the combination of methods would result in a sensitive method for detecting cancer. Applicant respectfully submits that the combined methods still fail to teach or suggest methods of detecting DNA markers in bone marrow sample, as required by claim 16.

Accordingly, Silva in view of Kawakami is not obvious over the present claim 16. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

Conclusion

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned at the Los Angeles, California telephone number (310) 785-4617 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Date: June 6, 2008

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